Ser... No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

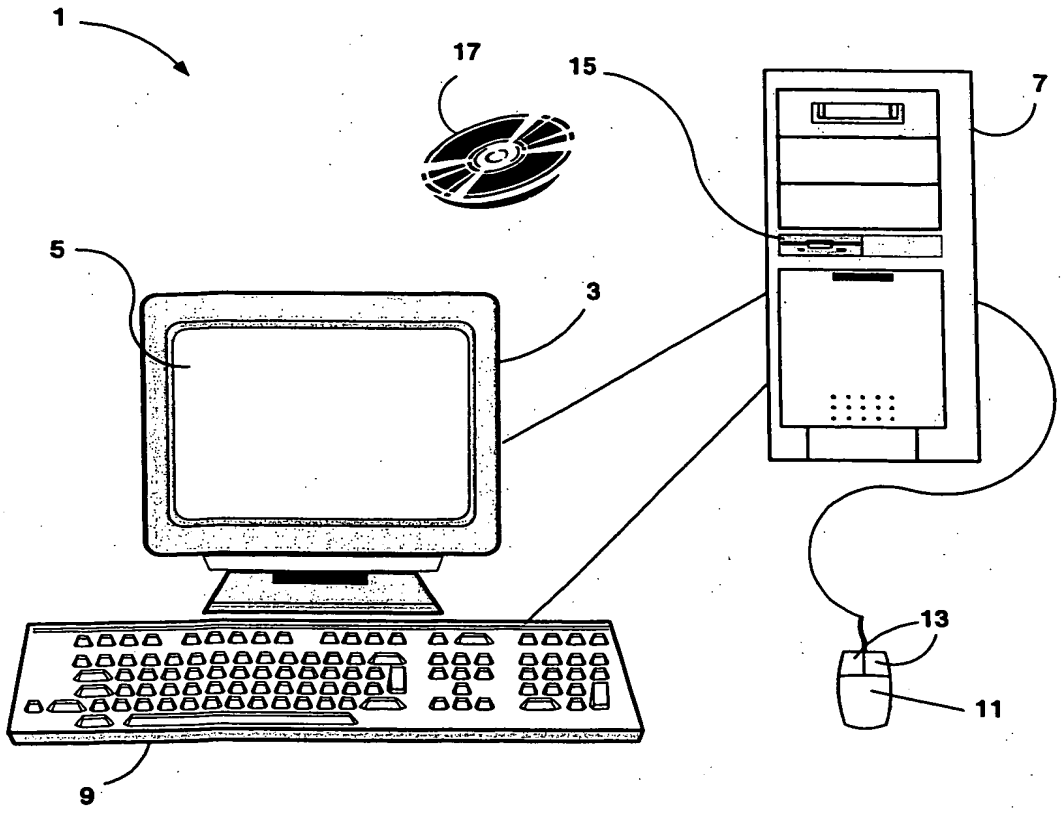


Figure 1

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

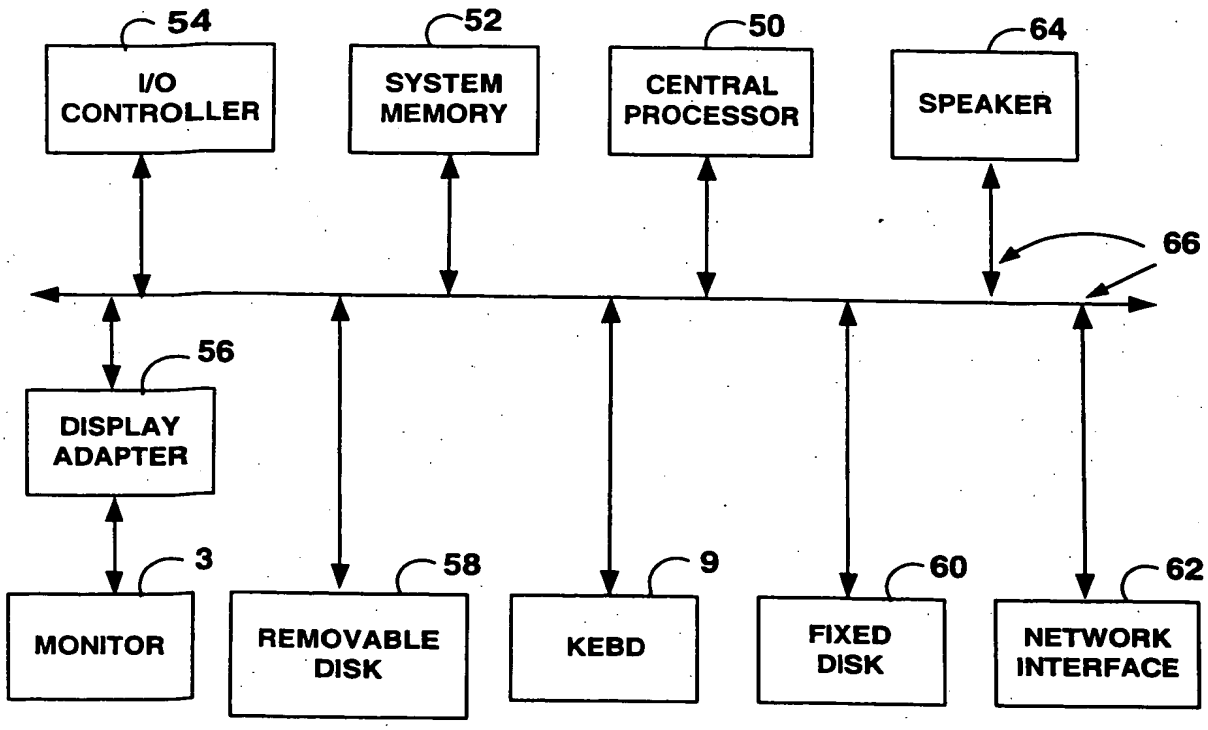
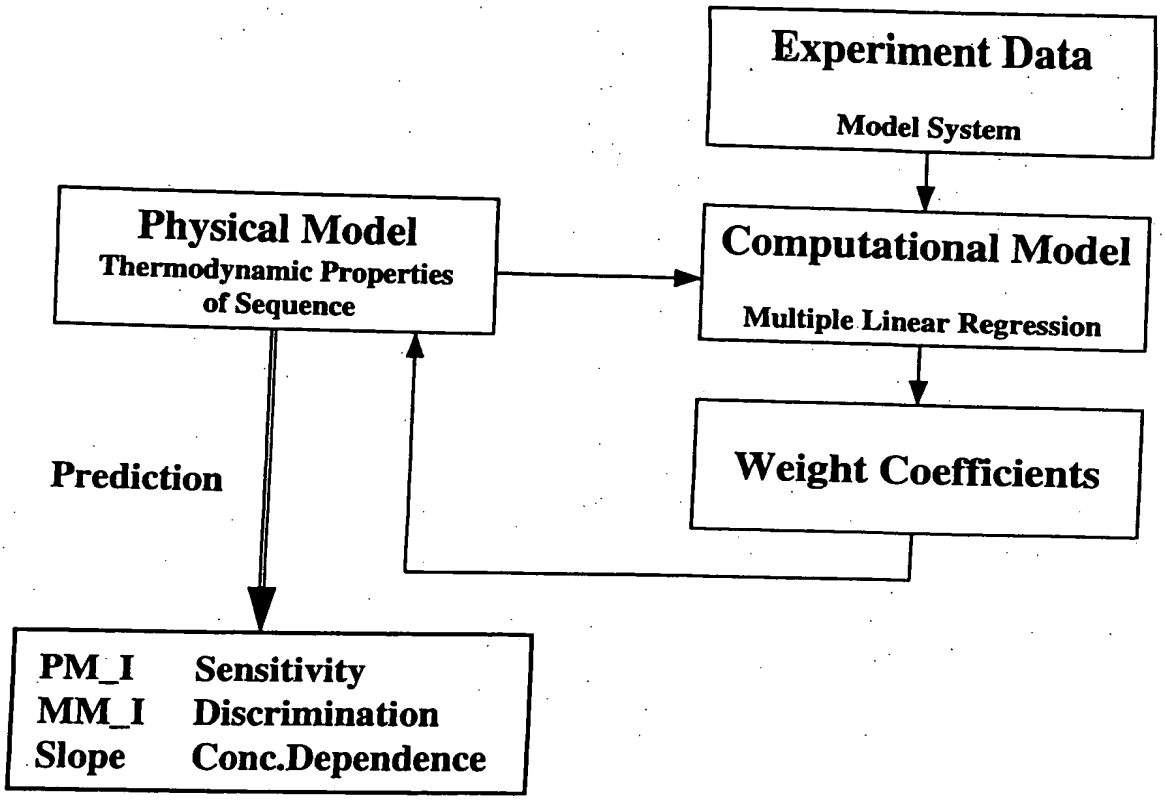


Figure 2

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Figure 3

Predicting Probe Quality



Basic Physical Model

$$P + T \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} P \cdot T$$

Figure 4

Define Each Nucleotide at Each position

Figure 5

Example : GTCA

***Using A as ref. 3 base/position**

i	Position	Base	S_i	
1	1	C	0	
2	1	G	1	(1st position is G)
3	1	T	0	
4	2	C	0	
5	2	G	0	
6	2	T	1	(2nd position is T)
7	3	C	1	(3rd position is C)
8	3	G	0	
9	3	T	0	
10	4	C	0	(4th position is A as reference)
11	4	G	0	
12	4	T	0	

Relative ΔG vs. Base Position

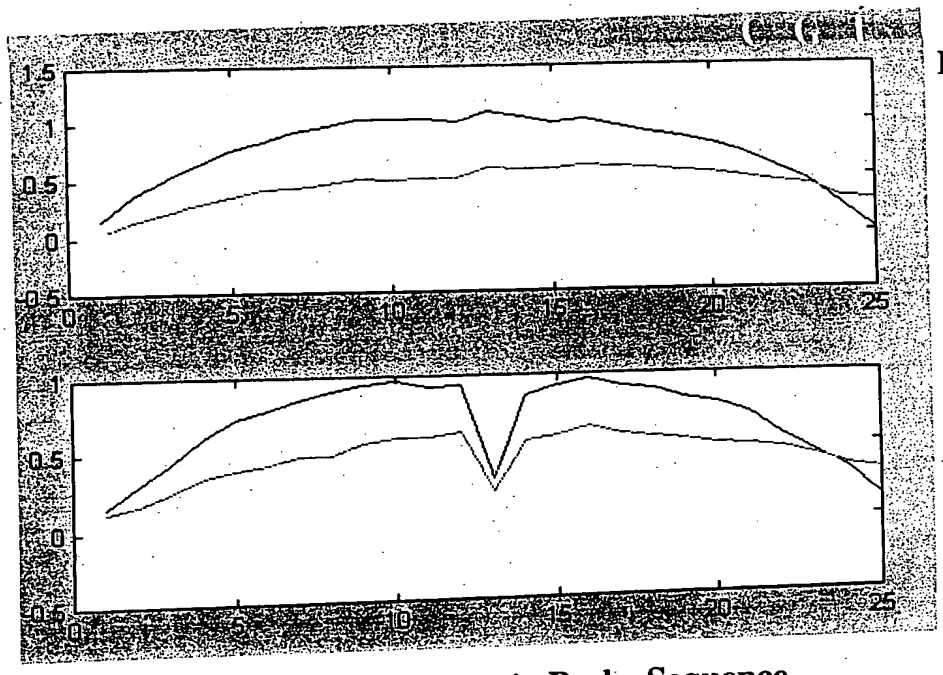


Figure 6A

PM

Figure 6B

MM

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Figure 7

Overall Reaction

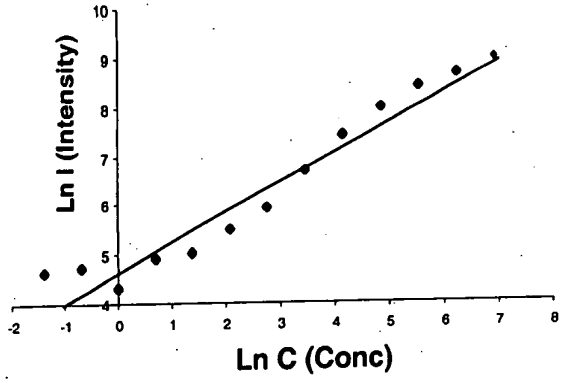
Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Concentration Dependence: Slope

Figure 8

$$\text{Ln } I = S * \text{Ln } C + \text{Ln } K_{app}$$

$$I = K_{app} * C^{S}$$



I: Intensity

K_{app}: Apparent Affinity Constant

C: Concentration

S: Empirical Value ($0 < S < 1$)

Relationship between Kapp vs. S

- Prediction of Probe Saturation

Figure 9A

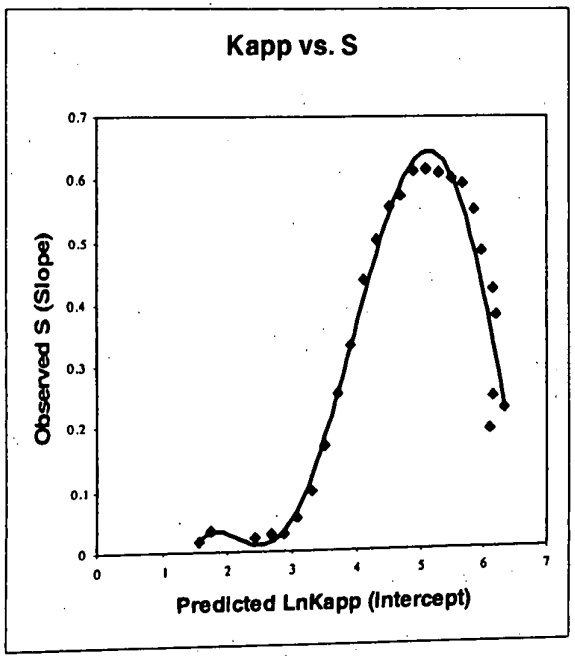
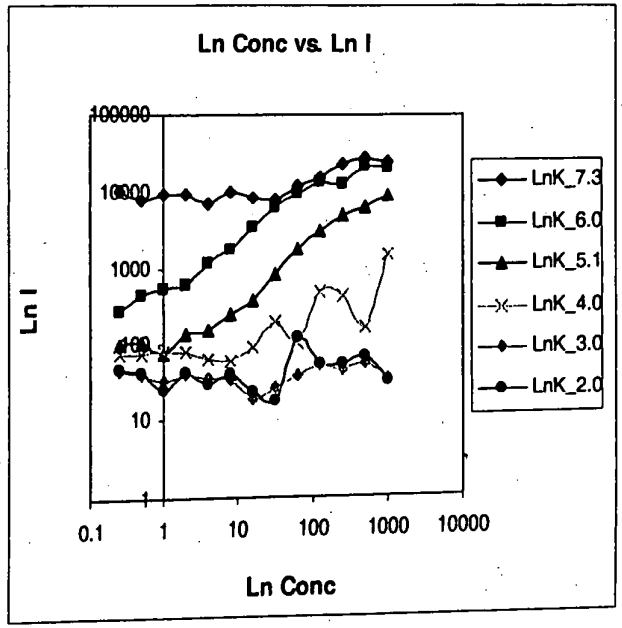


Figure 9B



S No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Serial No.: 09/718,295
Filing Date: November 21, 2000
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Docket No.: 3359/US

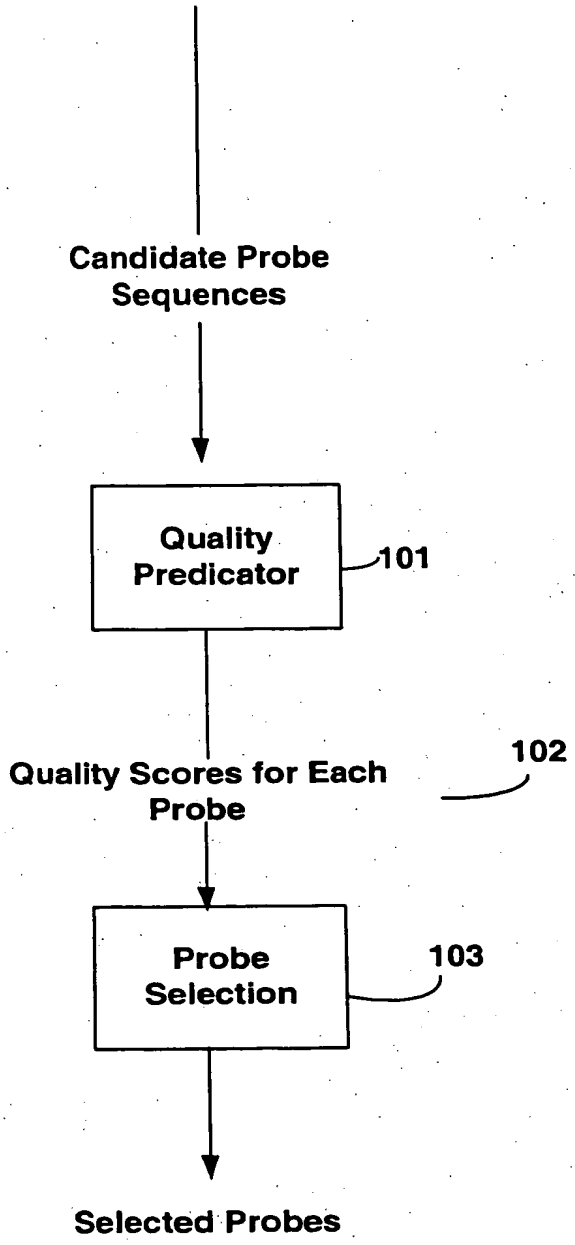


Figure 10

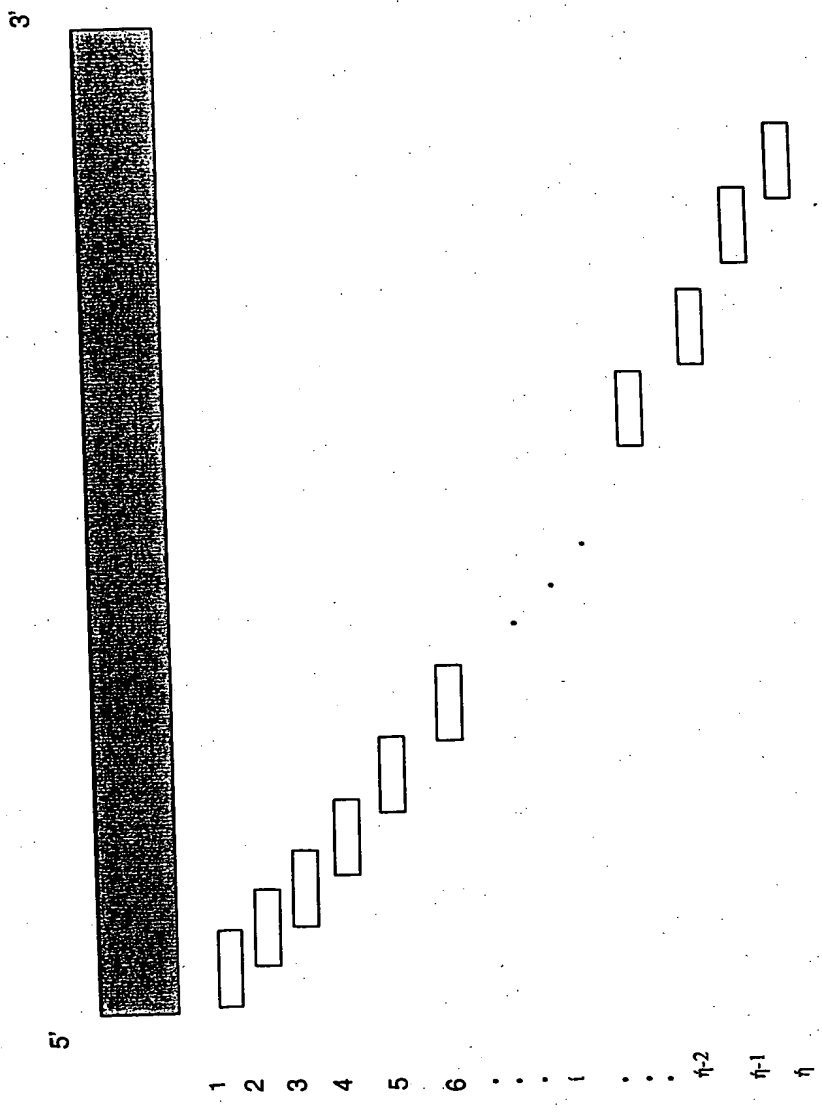


FIGURE 11

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

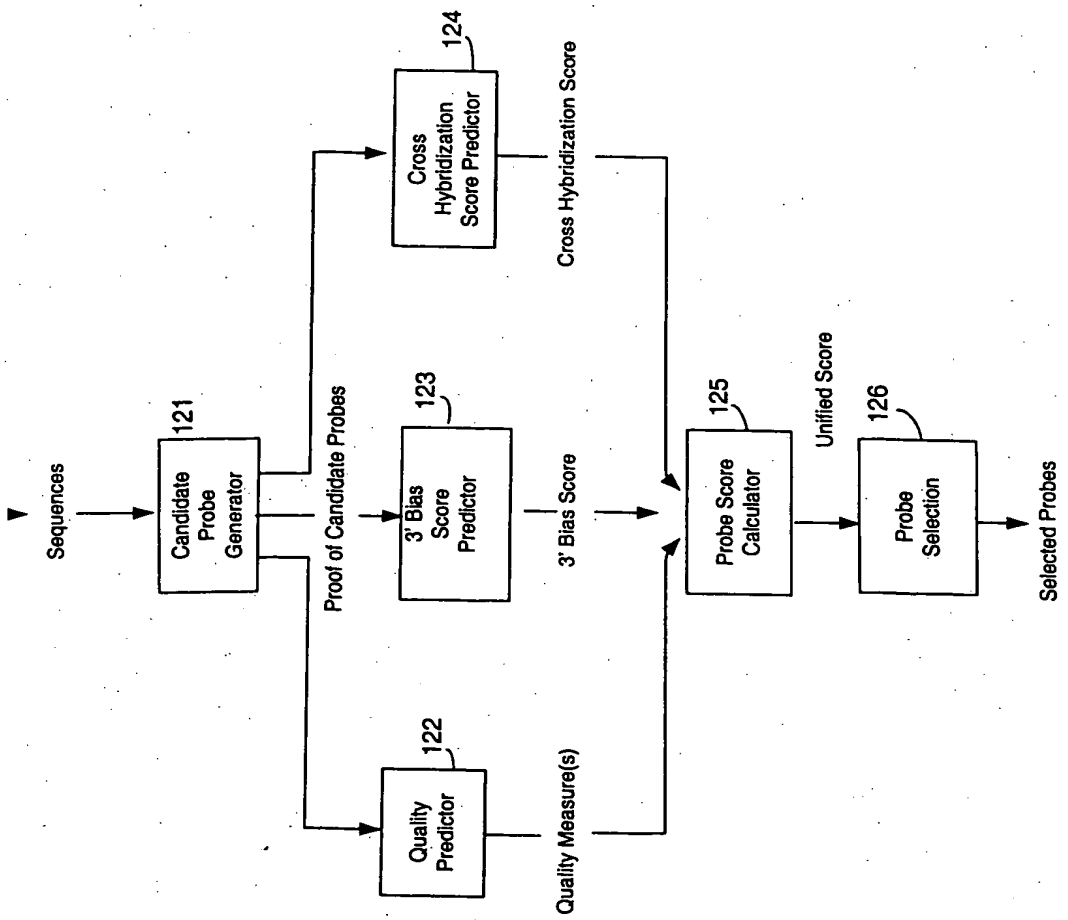


Figure 12

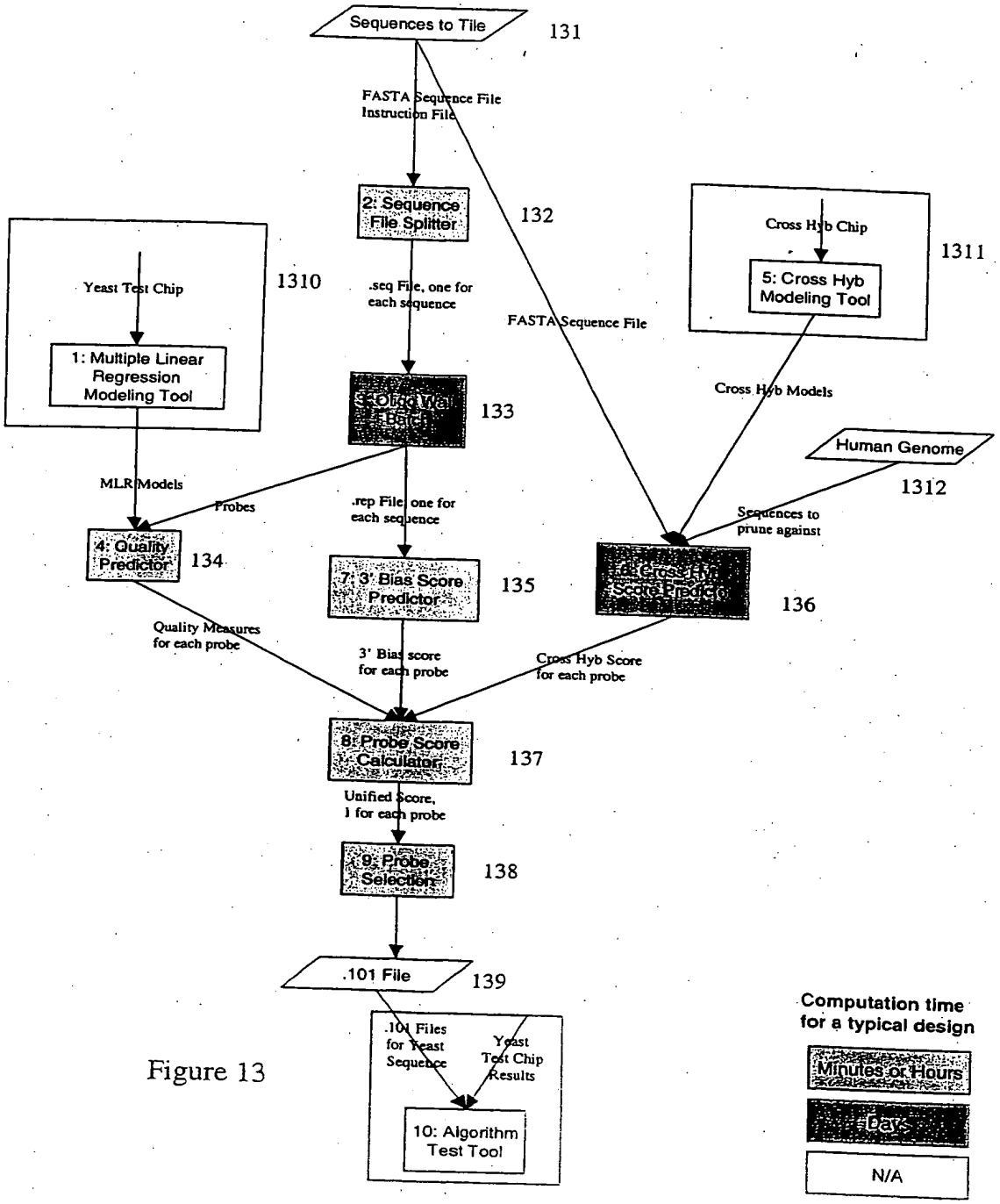

Sequences to Tile
131
FASTA Sequence File
Instruction File
2: Sequence File Splitter
132
Yeast Test Chip
1310
1: Multiple Linear Regression Modeling Tool
.seq File, one for each sequence
FASTA Sequence File
Cross Hyb Chip
1311
5: Cross Hyb Modeling Tool
Cross Hyb Models
3: Oligo Weight Batch
133
Human Genome
1312
MLR Models
Probes
.rep File, one for each sequence
Sequences to prune against
4: Quality Predictor
134
7: 3' Bias Score Predictor
135
6: Cross Hyb Score Predictor
136
Quality Measures for each probe
3' Bias score for each probe
Cross Hyb Score for each probe
8: Probe Score Calculator
137
Unified Score, 1 for each probe
9: Probe Selection
138
.101 File
139
.101 Files for Yeast Sequence
Yeast Test Chip Results
10: Algorithm Test Tool
Computation time for a typical design
Minutes or Hours
Days
N/A

Figure 13

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

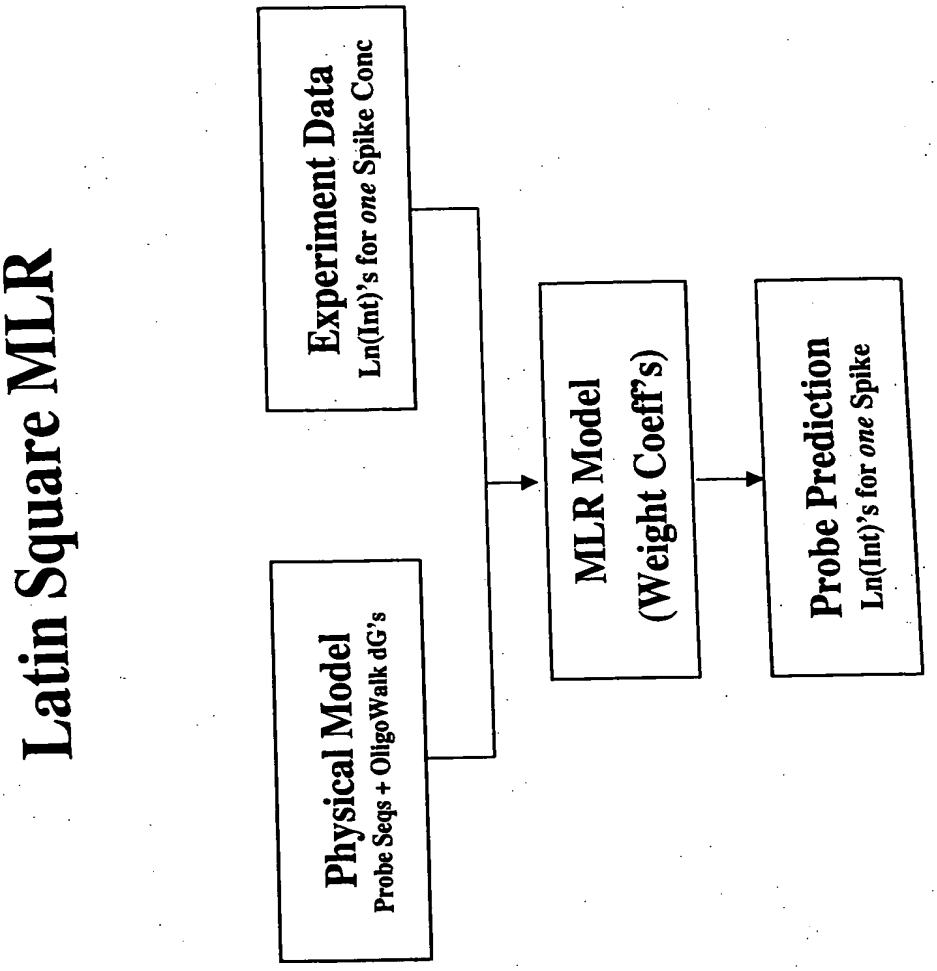


Figure 14

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

112 Yeast Clones Randomly Divided into 14 Groups

Groups

1	2	3	4	5	6	7	8	9	10	11	12	13	14
YNL259C	YNL037C	YAL038W	YHR044C	YMR127C	YLR377C	YOL064C	YPL209C	YIR034C	YJR148W	YEL046C	YGR185C	YBR166C	YOL156C
YEL003W	YDR113C	YLR083C	YJL117W	YNL290W	YOL086C	YJR094C	YFL029C	YMR276W	YML060W	YGR072W	YGL181W	YJL155C	YNL227C
YDL235C	YGL105W	YLL043W	YMR116C	YMR228W	YJR019C	YIR026C	YGR040W	YMR294W	YDL188C	YMR203W	YGL213C	YEL036C	YNL228W
YEL024W	YDR498C	YBR212W	YPL111W	YPR057W	YOR085W	YLR056W	YPR065W	YPL001W	YGR109C	YGR112W	YOL136C	YJL014W	YMR108W
YEL018W	YDL029W	YNL015W	YCL055W	YNR035C	YDL226C	YMR270C	YPR191W	YFL039C	YOL043C	YHR208W	YEL037C	YJL110C	YPL043W
YER161C	YKL081W	YOL078W	YFR025C	YCL032W	YBL016W	YBR018C	YMR139W	YNL307C	YLR291C	YIL136W	YHL022C	YEL056C	YLR153C
YKL193C	YFR053C	YML098W	YLR354C	YIL154C	YBL068W	YBR057C	YPR035W	YGL148W	YDR088C	YOR099W	YHL014C	YJR155W	YPR074C
YPR129W	YFL018C	YOL143C	YPL069C	YBR034C	YHR025W	YER118C	YNL005C	YGL155W	YNR015W	YOR176W	YKR061W	YNL111C	YPL089C

Figure 15

rial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Latin Square Experiment

Groups →

Exp ↓

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	0	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024
2	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	0
3	0.5	1	2	4	8	16	32	64	128	256	512	1024	0	0.25
4	1	2	4	8	16	32	64	128	256	512	1024	0	0.25	0.5
5	2	4	8	16	32	64	128	256	512	1024	0	0.25	0.5	1
6	4	8	16	32	64	128	256	512	1024	0	0.25	0.5	1	2
7	8	16	32	64	128	256	512	1024	0	0.25	0.5	1	2	4
8	16	32	64	128	256	512	1024	0	0.25	0.5	1	2	4	8
9	32	64	128	256	512	1024	0	0.25	0.5	1	2	4	8	16
10	64	128	256	512	1024	0	0.25	0.5	1	2	4	8	16	32
11	128	256	512	1024	0	0.25	0.5	1	2	4	8	16	32	64
12	256	512	1024	0	0.25	0.5	1	2	4	8	16	32	64	128
13	512	1024	0	0.25	0.5	1	2	4	8	16	32	64	128	256
14	1024	0	0.25	0.5	1	2	4	8	16	32	64	128	256	512

Figure 16

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Latin Square Data Sets from Yeast_Test_Hyb Chips

Lot 1 (9912072)

No Background:	3 Scans	14 chips	(530, PMT=701; 570, PMT=701; 570, PMT=600)
+ Background:	3 Scans	14 chips	(530, PMT=701; 570, PMT=701; 570, PMT=600)

Lot 2 (9910426)

No Background:	1 Scan	14 chips	(570, PMT=600)
No Background:	1 Scan	14 chips	(570, PMT=600)

Lot 3 (9910427)

+ Background:	1 Scan	14 chips	(570, PMT=526)
No Background_Rep1:	1 Scan	14 chips	(570, PMT=526)
No Background_Rep2:	1 Scan	14 chips	(570, PMT=526)

Lot 4 (9913514)

No Background:	1 Scan	14 chips	(570, PMT=526)
+ Background:	1 Scan	14 chips	(570, PMT=526)

Lot 5 (9914059)

+ Background_Rep1:	1 Scan	14 chips	(570, PMT=526)
+ Background_Rep2:	1 Scan	14 chips	(570, PMT=526)
No Background:	1 Scan	14 chips	(570, PMT=526)

Figure 17

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

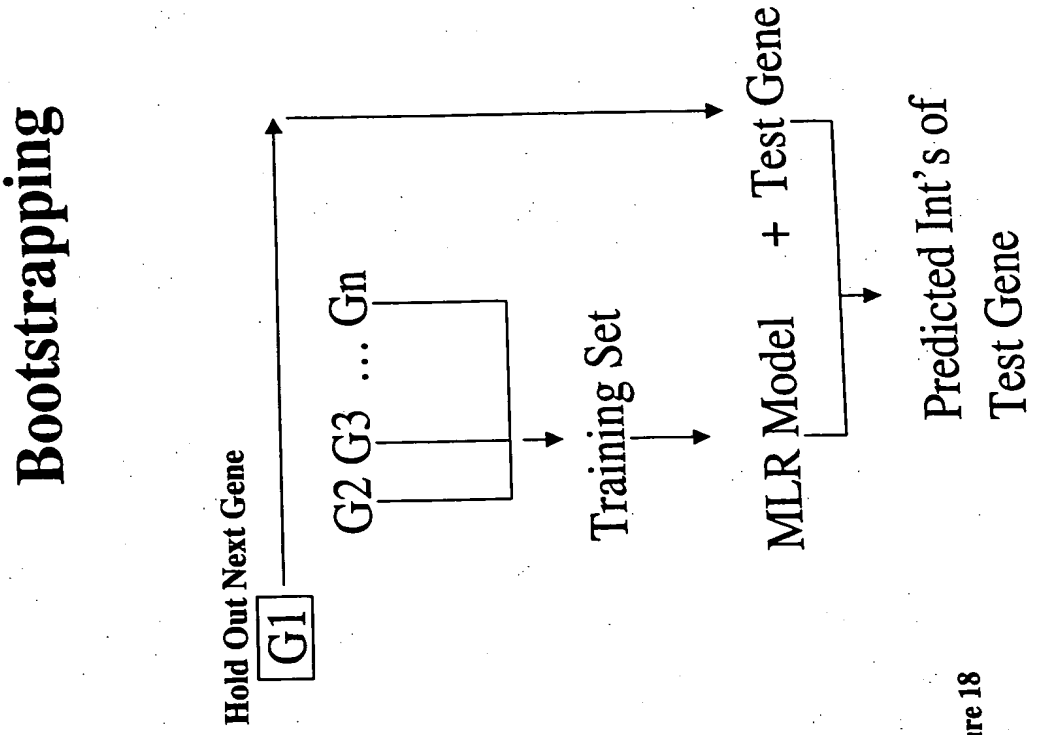


Figure 18

Ser. No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Figure 19A

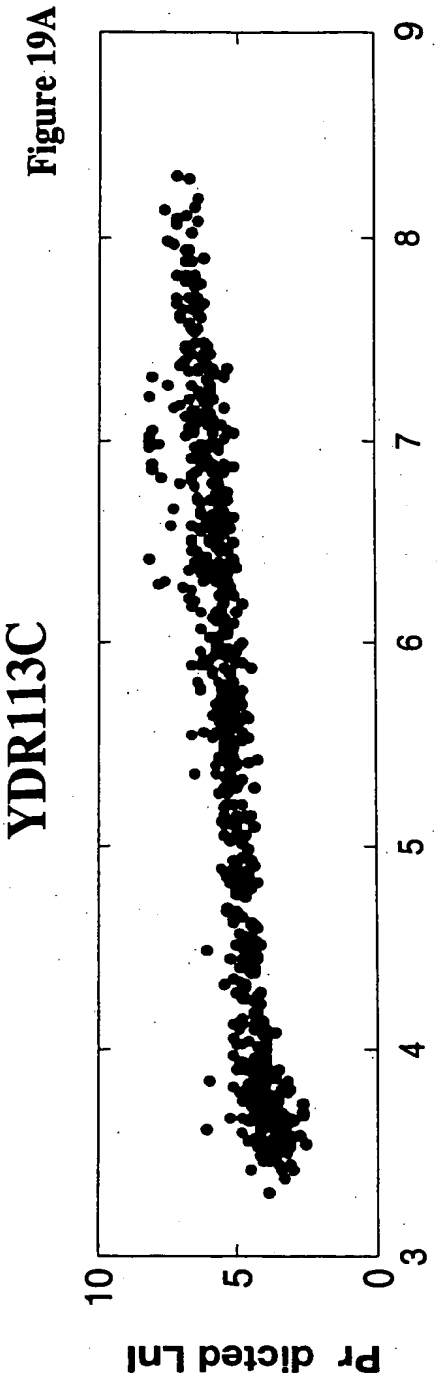
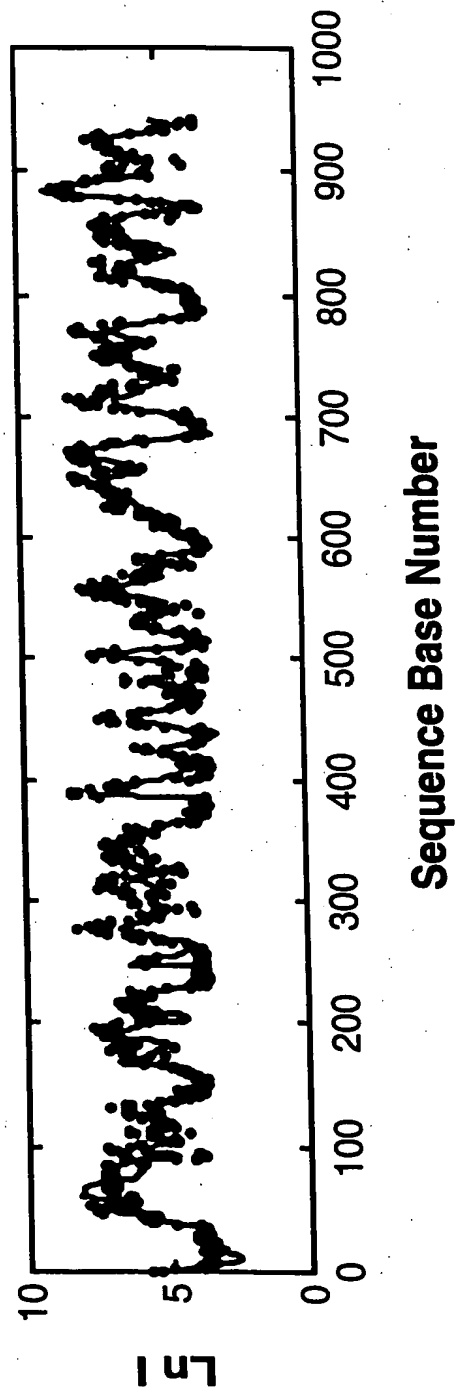


Figure 19B



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Filing Date: November 21, 2000
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Docket No.: 3359/US

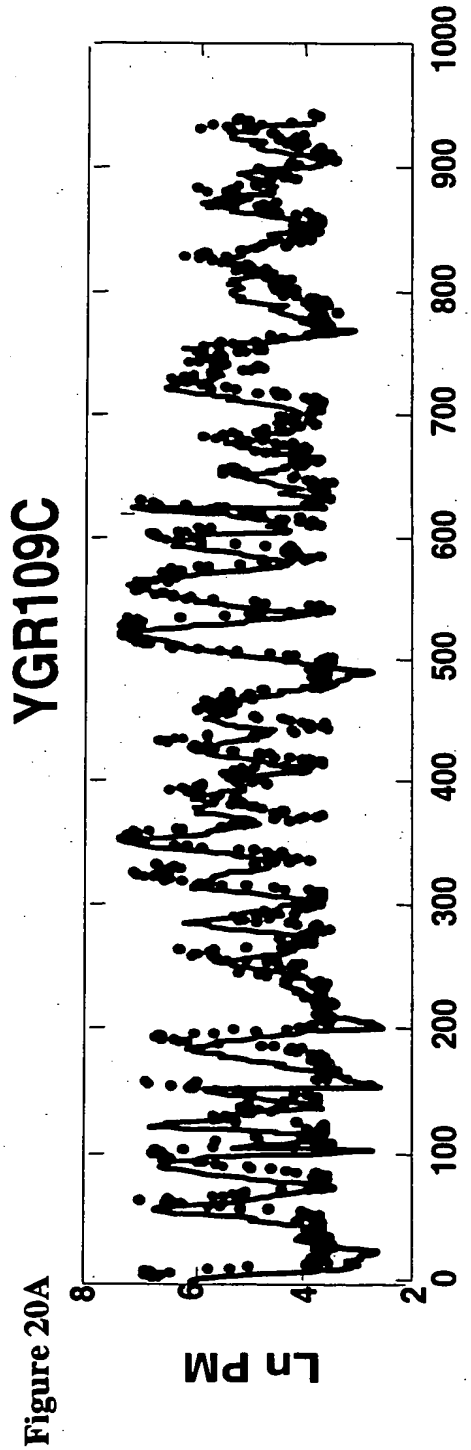


Figure 20A

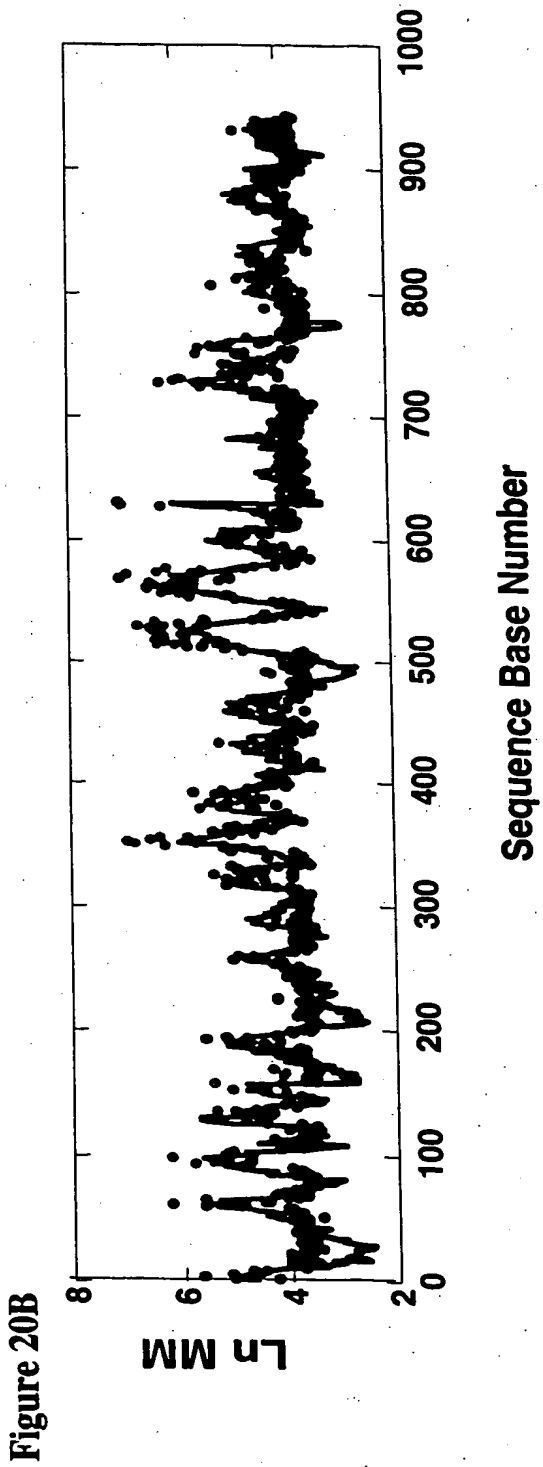


Figure 20B

Ln(Int) at Different Spike Concentrations

Figure 21

Correlation between Predicted & Observed Ln(Int)'s

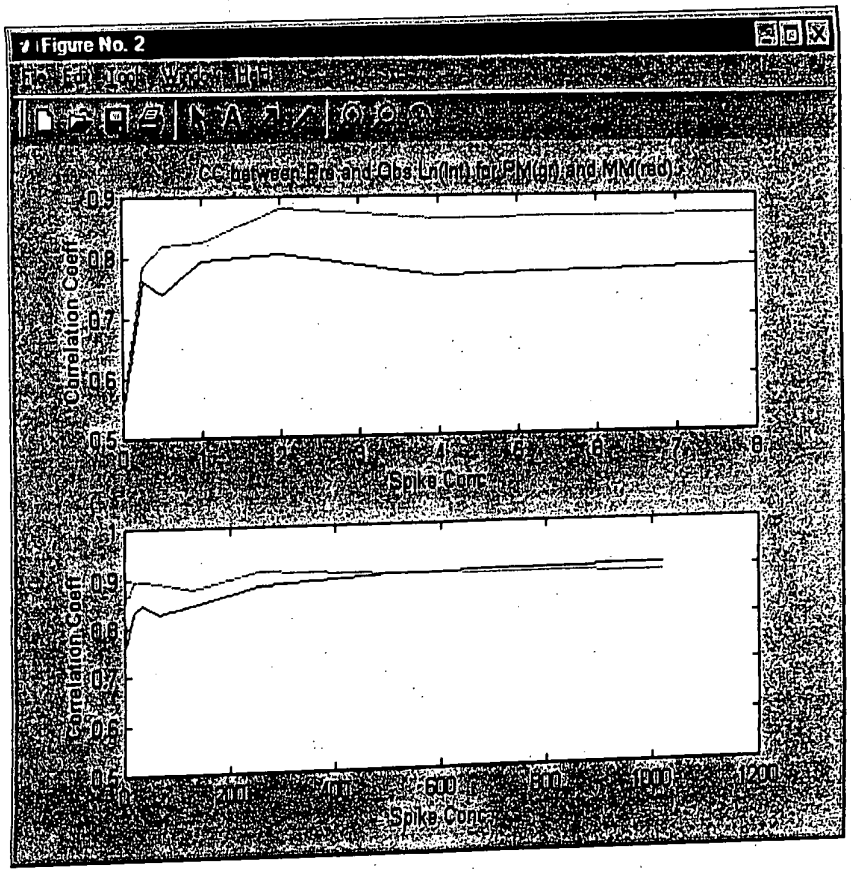


Figure 22

Serial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

Negative Control: Gene in Wrong Orientation

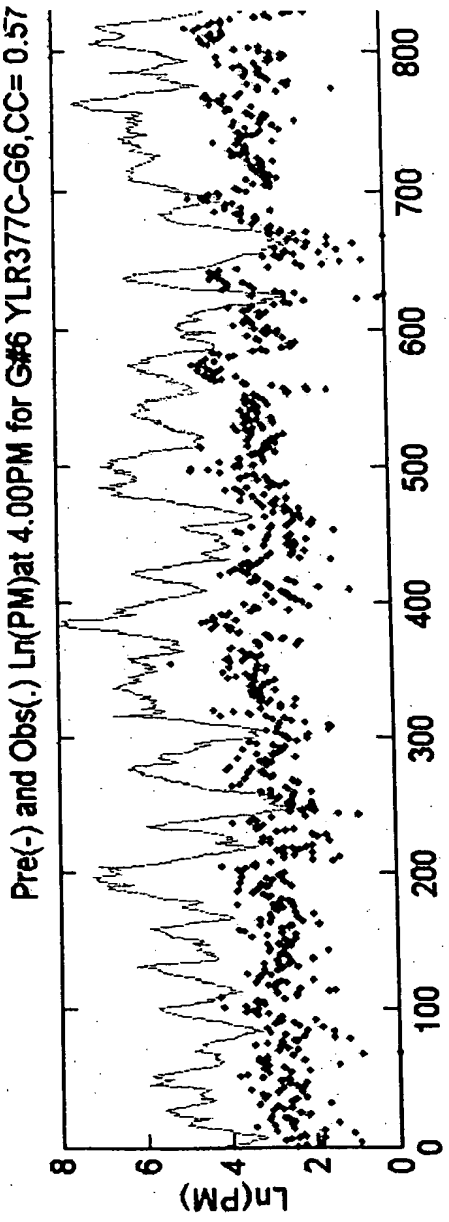


Figure 23

Predicted Observed Slopes

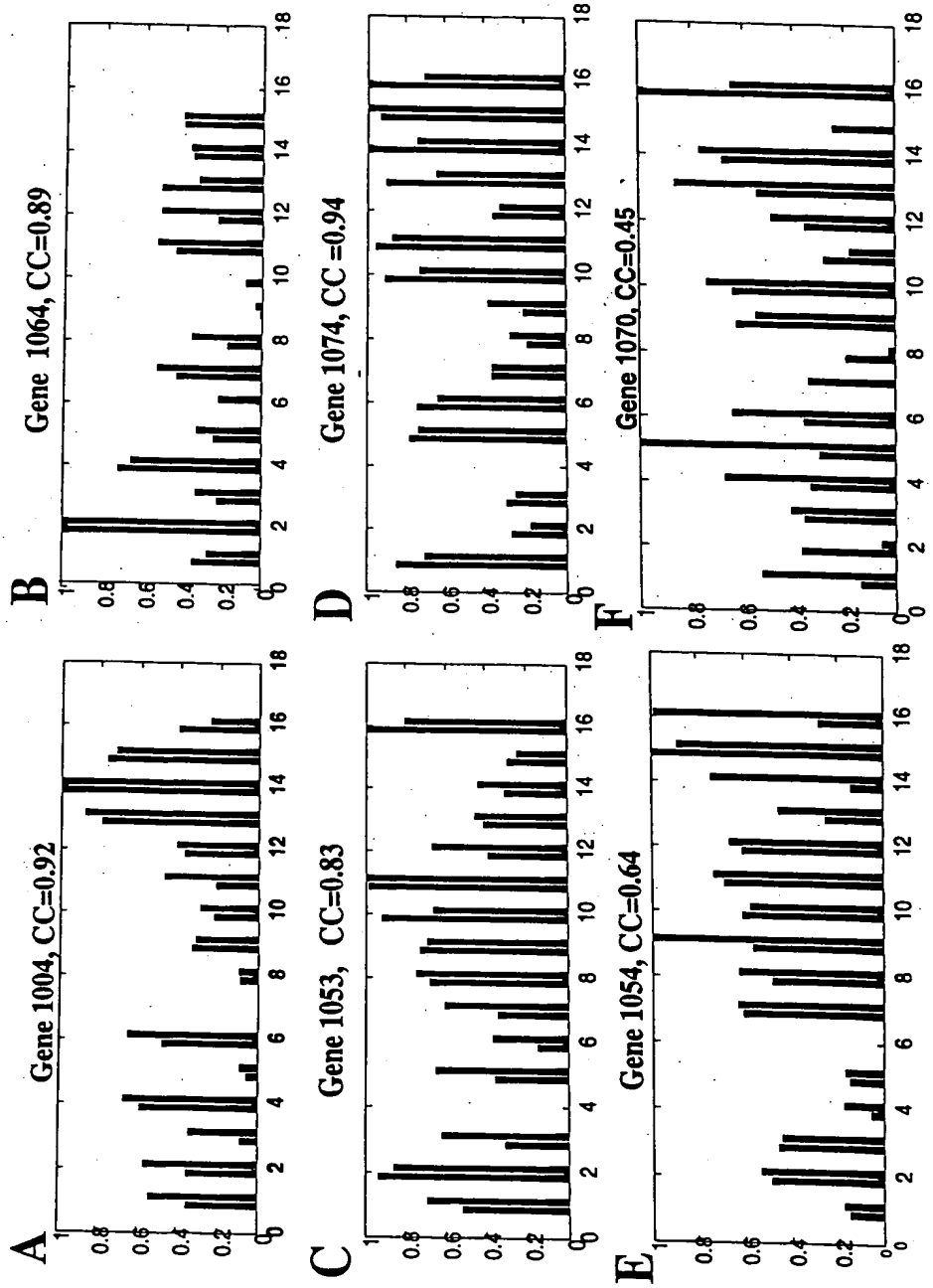
Figure 24

erial No.: 09/718,295
Filing Date: November 21, 2000
Inventors: Rui Mei
Docket No.: 3359/US

From Yeast to Human

Figure 25

Using Parameters from Yeast Model System to Predict Human_U95A



Predictions for Hu_U95a Probe Sets

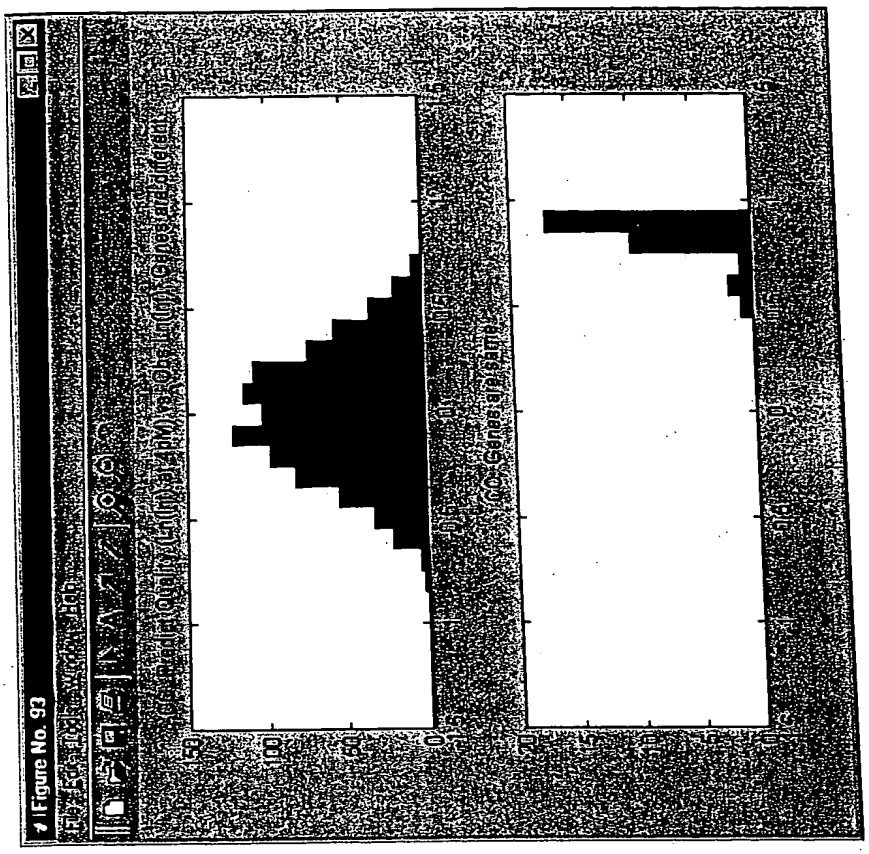


Figure 26

Sixteen Probes Selected By Dynamic Programming Algorithm

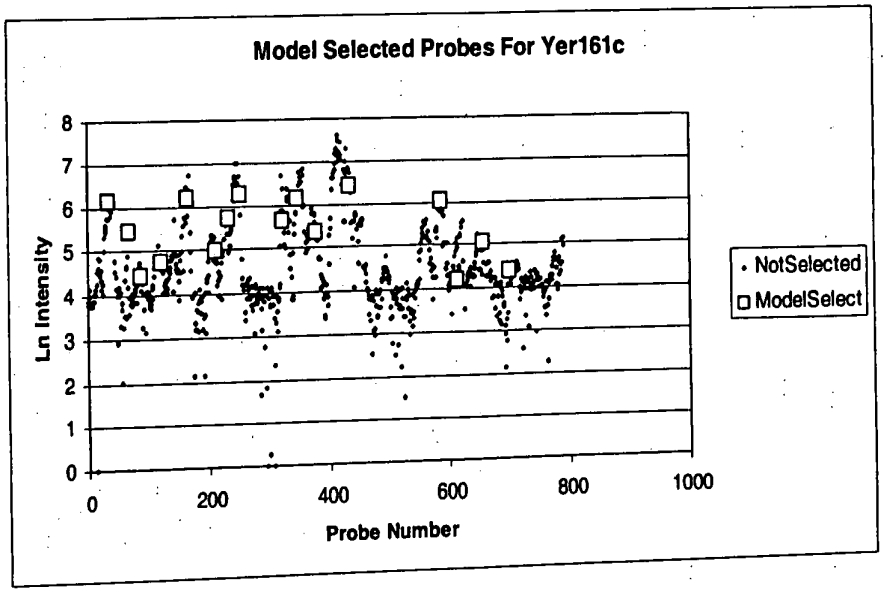


Figure 27

Comparison of AveDiff Values of all Yeast Test Chip Genes:New vs Random vs Rules Selection

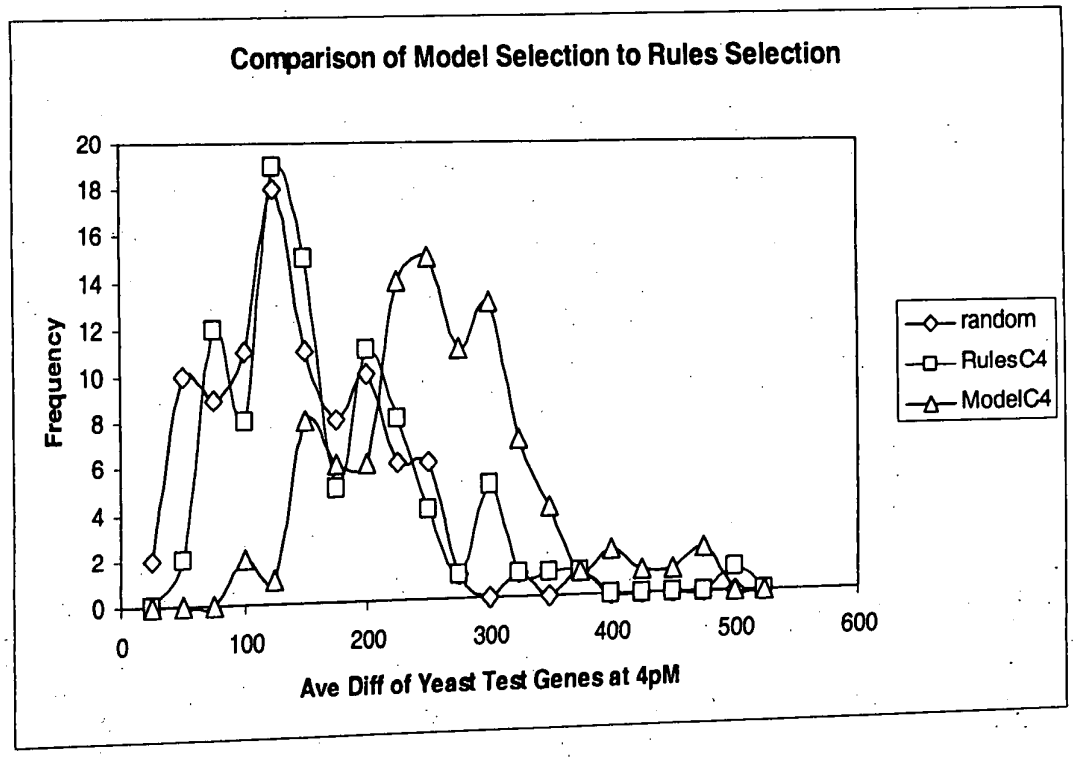


Figure 28